REMARKS

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification is asserted not to be enabling for the groups X_1, Y_1 and Y_2 being either sulfur or nitrogen instead of the admittedly enabled oxygen. This ground of rejection is respectfully traversed.

Initially, in examining a patent application, the Patent Office is required to assume that the specification complies with the enablement requirements of Section 112 unless it has "acceptable evidence or reasoning" to suggest otherwise. The Patent Office must provide reasons supported by the record why the specification is not enabling. Then and only then does the burden shift to the applicant.[1] The Examiner has merely made a conclusory statement of non-compliance with Section 112 without acceptable evidence or reasoning, and thus the rejection under Section 112 is improper and should be withdrawn.

In any event, the applicant asserts that the specification is enabling. The original claims are part of the disclosure. The original claims included the groups X_1, Y_1 and Y_2 being either oxygen, sulfur or nitrogen. Having the groups X_1, Y_1 and Y_2 be either sulfur or nitrogen instead of oxygen, accordingly, was clearly taught in the application as filed. Examples are set out in the specification of the compounds as defined in the original claims wherein the groups X_1, Y_1 and Y_2 are oxygen. Whether the disclosure is enabling is a question of what was known to those of ordinary skill in the art at the time the application was filed. A specification need not contain a working example of every compound claimed if the invention is described in such a manner that one skilled in the art would be able to practice it without undue experimentation.[2] If it was known that either sulfur or nitrogen could be used in place of oxygen for the groups X_1, Y_1 and Y_2 in the methods of synthesis disclosed in the specification, then the examples demonstrating oxygen coupled with the disclosure in the original claims of sulfur and nitrogen being alternatives for oxygen satisfies the requirements of the first paragraph of 112. The claims do not need to be limited to the preferred embodiments in order to satisfy the enablement requirement.[3]

The prior art is abundant with teaching of the known substitutability of sulfur and nitrogen for oxygen for the groups X_1, Y_1 and Y_2 in the synthesis steps described in the

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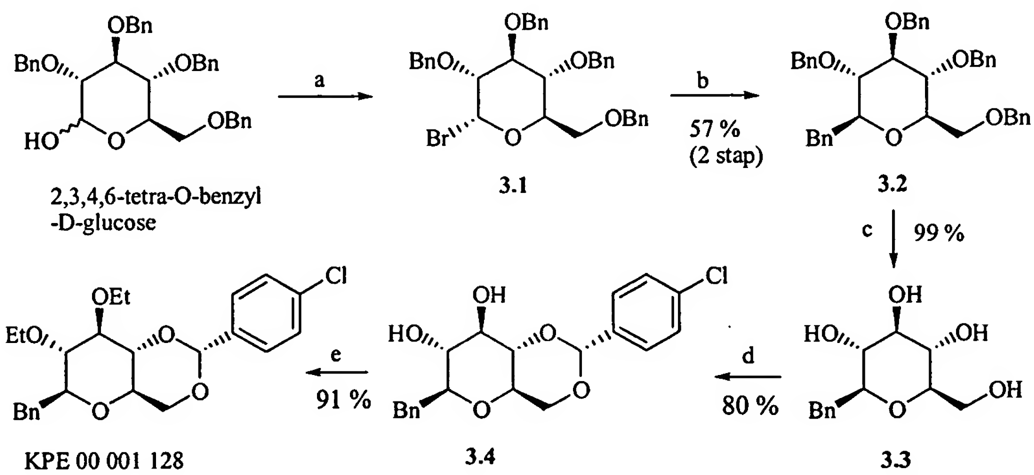
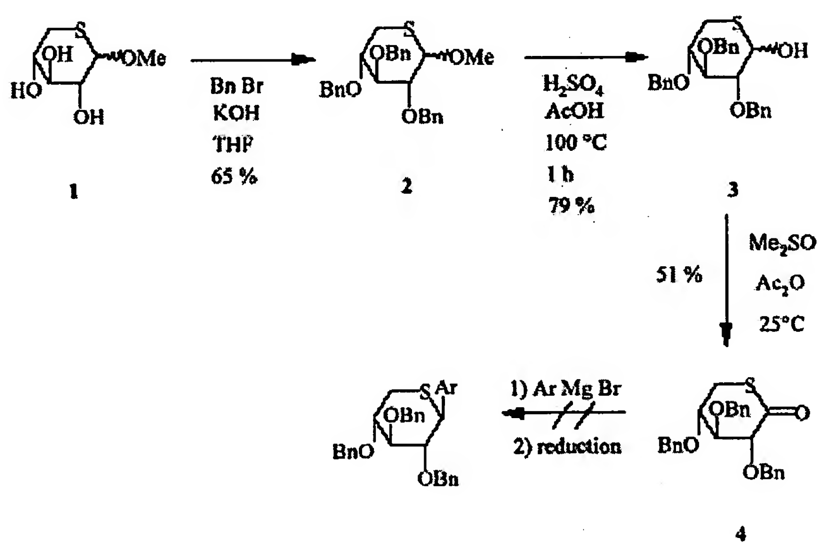
[1] Gould v. Mossinghoff, 229 U.S.P.Q. 1 (D.C. 1985)
[2] In re Borkowski and Van Venrooy, 164 U.S.P.Q. 642 (C.C.P.A. 1970)
[3] Ex parte Gould, 6 U.S.P.Q.2d 1680 (Bd. Pat. App. 1987)

specification. With respect to the X_1 group, the synthesis pathway is described in the text of the specification and shown in Fig. 4 of the application, which is reproduced below:



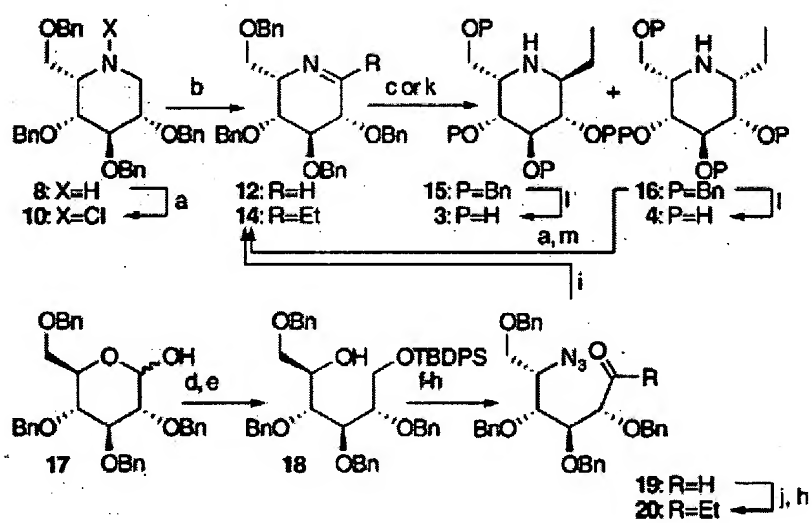
Specifically, compounds similar to compounds 3.2 and 3.3 of Fig. 4 wherein the carbohydrate oxygen group (X_1) has been substituted with sulfur are known in the art. The enclosed article, Mignon, L., et al., New 1-*C*-(5-thio-D-xylopyranosyl) derivatives as potential orally active venous antithrombotics, *J Carbohydrate Research* 338 **2003**, 1271-82, teaches the synthesis of such compounds in Scheme 1, reproduced below:



Scheme 1.

This paper illustrates approaches to introduce an 1-alkyl or aryl substituent at C-1 of a 5-thiosugar, using an analogous approach as described in the present application for the pyranose series, based on the nucleophilic substitution of a bromide or a trichloroacetimidate. Synthesis of 5-thiosugars is known in literature: for the synthesis of e.g. 5-thio-D-glucose, see: C.-W. Chiu, R.L. Whistler, *J. Org. Chem.*, **1973**, 832-834 (copy enclosed).

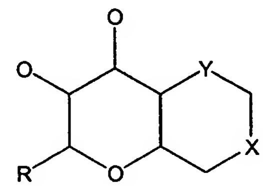
Similarly, the enclosed article Maugham, M., et al., Nitorgen Inversion as a Diastereomeric Relay in Azasugar Synthesis: The First Synthesis of Adenophorine, *Angew. Chem. Int. Ed.* 42 **2003**, 3788-92, teaches similar synthesis steps wherein nitrogen has been substituted for the carbohydrate oxygen, as illustrated in scheme 3, reproduced below:



This paper describes two approaches to the synthesis of 1-alkyl-iminosugar derivatives (Scheme 3). The most general approach starts from a hexopyranose sugar and allows for introduction of an alkyl group at C-1 via nucleophilic addition. The nitrogen is introduced as an azide via an S_N2-substitution reaction (Mitsunobu O., *Synthesis,* **1981**, 1), followed by Staudinger reduction and concomitant spontaneous cyclic imine formation, and reduction of the imine to the amine. The second approach starts from an iminosugar, which is oxidized with N-bromosuccinimide to a cyclic imine, followed by nucleophilic addition with a Grignard reagent or an organolithium to introduce the alkyl side chain at C-1. Each separate step is commonly used in this field and is well-known to anyone skilled in the art, and can even be found in text books such as J. March, *Advanced Organic Chemistry* (Wiley). For another example of the introduction of an azide,

Staudinger reduction and cyclization via reductive amination, see: S.P. Chavan, C. Praveen, Tetrahedron Lett., (2004) 45, 421-423 (copy attached). A list of references with other examples (limited to those containing a C-1 substituent) is attached.

With respect to the substitution of sulfur or nitrogen for the oxygen in the Y_1 and Y_2 groups, bicyclic acetal structures (see below)



wherein X = S, Y = O and wherein X = O, Y = S are known in the literature. Examples can be found in: E. Cabianca *et al., Tetrahedron Lett.*, **2003**, *44*, 5723-5725 (copy enclosed); A. Classen *et al., Liebigs Ann. Chem.*, **1993**, 183-187 and references cited therein.
Equally, bicyclic acetal structures wherein X = NR, Y = O, X = O, Y = NR; X = NR, and Y = NR' are known. Examples can be found in: K.Y. Ko *et al., Tetrahedron Lett.*, **1997**, *38*, 407-410; F.W. Lichtenthaler *et al., J. Org. Chem.*, **1974**, *39*, 1457-1462; J. Gelas *et al., Carbohydr. Res.*, **1997**, *299*, 253-269 (copies enclosed) and references cited therein.

A thiol group can be introduced using well-known procedures, such as by transformation of a hydroxyl group in a good leaving group (e.g. a mesylate, a triflate or an iodide), followed by substitution with potassium thioacetate and saponification, or directly on an alcohol by Mitsunobu substitution with a thioacid followed by saponification. A list with examples for introduction of a thiol group at C-4 is attached (ring-O-4-S-introduction.rtf). Examples can be found *inter alia* in: D. Crich *et al., J. Org. Chem.*, **2000**, *65*, 801-805; S.G. Withers *et al., Ang. Chem. Int. Ed. Engl.*, **2003**, *42*, 352-354; J.-M. Beau *et al., Tetrahedron*, **1995**, *51*, 3205-3220 and references cited therein.

A list with examples for introduction of a thiol group at C-6 is also attached (ring-O-6-S-introduction.rtf). Specific examples can be found *inter alia* in: R.J.K. Taylor *et al., Eur. J. Org. Chem.*, **2002**, 1323-1336; Y. Ito *et al., J. Org. Chem.*, **2003**, *68*, 5602-5613 and references cited therein.

Amino groups at C-4 and C-6 are mostly introduced by substitution of a good leaving group (mesylate, triflate) with sodium azide in DMF, followed by reduction (catalytic

hydrogenation, or Staudinger reduction with a phosphine). These procedures are well-known to anyone skilled in the art. A list of selected references is attached (ring-O-6or4-N-introduction.rtf). Examples can be found *inter alia* in: J.S. Thorson *et al., Org. Lett.*, **2003,** *5,* 2223-2226; T. Baasov *et al., Org. Lett.*, **2003,** *5,* 3575-3578; C.-W. Tom Chang *et al., Org. Lett.*, **2003,** *5,* 431-434; P.H. Seeberger *et al., Synlett,* **2003,** 1323-1326 and references cited therein.

Having such compounds, one only needs to follow the steps described in the specification to synthesize the claimed compounds wherein sulfur and nitrogen have been substituted for oxygen. The application clearly discloses the substitution of sulfur or nitrogen for the X_1, Y_1 and Y_2 groups and contains example of the compounds wherein oxygen is present. The teachings of the prior art are sufficient to allow a person of ordinary skill in the art to practice the claimed invention, that is substitute sulfur or nitrogen for oxygen at the X_1, Y_1 and Y_2 groups without undue experimentation. The rejection for lack of enablement should be reconsidered and withdrawn.

Claims 4 and 5 have been amended to address the objection raised by the Examiner.

Accordingly, the purpose of the claimed invention is not taught nor suggested by the cited references, nor is there any suggestion or teaching which would lead one skilled in the relevant art to combine the references in a manner which would meet the purpose of the claimed invention. Because the cited references, whether considered alone, or in combination with one another, do not teach nor suggest the purpose of the claimed invention, Applicant respectfully submits that the claimed invention, as amended, patentably distinguishes over the prior art, including the art cited merely of record.

Based on the foregoing, Applicant respectfully submits that its claims 1-6 are in condition for allowance at this time, patentably distinguishing over the cited prior art. Accordingly, reconsideration of the application and passage to allowance are respectfully solicited.

The Examiner is respectfully urged to call the undersigned attorney at (515) 288-2500 to discuss the claims in an effort to reach a mutual agreement with respect to claim limitations in the present application which will be effective to define the patentable subject matter if the present claims are not deemed to be adequate for this purpose.

Respectfully submitted,

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